

WHAT IS CLAIMED IS:

1. A process of treating oral leukoplakia lesions of humans in need of such treatment, the process comprising the step of applying topically to the leukoplakia lesion an effective amount of a clear aqueous formulation comprising:

water;

a water miscible pharmaceutically acceptable polyol;

a pharmaceutically acceptable unsaturated fatty acid ester;

a pharmaceutically acceptable surfactant, and

$\beta$ -carotene, said  $\beta$ -carotene being in a micellized form within said formulation.

2. A process in accordance with Claim 1 wherein the formulation additionally comprises a pharmaceutically acceptable anti-oxidant.

3. A process in accordance with Claim 2 wherein the pharmaceutically acceptable anti-oxidant is d-alpha-tocopherol or a pharmaceutically acceptable derivative of d-alpha tocopherol having vitamin E activity.

4. A process in accordance with Claim 1 wherein the formulation additionally comprises a compound having vitamin A activity.

5. A process in accordance with Claim 1 wherein the surfactant is polyethoxylated castor oil.

1                   6. A process in accordance with Claim 1 wherein the polyol is  
2 glycerol.

3                   7. A process in accordance with Claim 1 wherein the unsaturated fatty  
4 acid ester is ethyl linoleate.

5                   8. A process in accordance with Claim 1 wherein the formulation is a  
6 gel.

7                   9. A process in accordance with Claim 8 comprising the steps of  
8 applying the gel to the leukoplakia lesion at least twice a day.

9                   10. A process in accordance with Claim 1 wherein the formulation  
10 comprises:

11                   10 to 50 % by weight water;

12                   5 to 40 % by weight of the water miscible pharmaceutically acceptable  
13 polyol;

14                   1 to 20 % by weight of the pharmaceutically acceptable unsaturated  
15 fatty acid ester;

16                   10 to 60 % by weight of the pharmaceutically acceptable surfactant,  
17 and

18                   0.03 to 9.0 % by weight of  $\beta$ -carotene.

19                   11. A process in accordance with Claim 10 wherein the water miscible  
20 pharmaceutically acceptable polyol is glycerol;

1 the pharmaceutically acceptable unsaturated fatty acid ester is ethyl  
2 linoleate, and

3 the pharmaceutically acceptable surfactant is polyethoxylated castor oil.

4 12. A process in accordance with Claim 1 wherein the formulation  
5 comprises:

6 20 to 40 % by weight water;

7 10 to 30 % by weight of the water miscible pharmaceutically  
8 acceptable polyol;

9 1 to 15 % by weight of the pharmaceutically acceptable unsaturated  
10 fatty acid ester;

11 20 to 40 % by weight of the pharmaceutically acceptable surfactant,  
12 and

13 0.3 to 3.0 % by weight of  $\beta$ -carotene.

14 13. A process in accordance with Claim 12 wherein the water miscible  
15 pharmaceutically acceptable polyol is glycerol;

16 the pharmaceutically acceptable unsaturated fatty acid ester is ethyl  
17 linoleate, and

18 the pharmaceutically acceptable surfactant is polyethoxylated castor oil.

19 14. A process in accordance with Claim 13 wherein the formulation  
20 additionally comprises d-alpha-tocopherol and a compound having vitamin A

1 activity.

2 15. A process in accordance with Claim 14 wherein the formulation is  
3 a gel.

4 16. A process in accordance with Claim 15 comprising the steps of  
5 applying the gel to the leukoplakia lesion at least twice a day.

6 17. A process in accordance with Claim 1 wherein the formulation  
7 comprises:

8 50 to 95 % by weight water;

9 1 to 10 % by weight of the water miscible pharmaceutically acceptable  
10 polyol;

11 0.01 to 2 % by weight of the pharmaceutically acceptable unsaturated  
12 fatty acid ester;

13 0.01 to 5 % by weight of the pharmaceutically acceptable surfactant,  
14 and

15 0.003 to 1.2 % by weight of  $\beta$ -carotene,

16 1 to 10 % by weight of a pharmaceutically acceptable sweetener;

17 0.01 to 2% of a pharmaceutically acceptable antibacterial agent;

18  
19 d -alpha tocopherol or a pharmaceutically acceptable derivative of d-  
20 alpha tocopherol having vitamin E activity;

1 vitamin A palmitate or a pharmaceutically acceptable derivative of  
2 vitamin A palmitate having vitamin A activity;  
3 a pharmaceutically acceptable chelating agent;  
4 a pharmaceutically acceptable antifoaming agent;  
5 a flavoring agent, and  
6 a preservative.

7 18. A process in accordance with Claim 17 wherein the water miscible  
8 pharmaceutically acceptable polyol is glycerol;

9 the pharmaceutically acceptable unsaturated fatty acid ester is ethyl  
10 linoleate;

11 the pharmaceutically acceptable surfactant is polyethoxylated castor  
12 oil;

13 the pharmaceutically acceptable sweetener is xylitol;

14 the pharmaceutically acceptable antibacterial agent is cetyl pyridinium  
15 chloride;

16 the pharmaceutically acceptable chelating agent is disodium EDTA,  
17 and

18 the preservative is sodium benzoate.

19 19. A process in accordance with Claim 18 wherein the formulation is  
20 an oral rinse.

1                   **20.** A process in accordance with Claim 19 wherein the formulation  
2 comprises:

3                   75 to 95 % by weight water;  
4                   2 to 7 % by weight of glycerol;  
5                   0.01 to 0.5 % by weight ethyl linoleate;  
6                   0.01 to 1 % by weight polyethoxylated castor oil;  
7                   0.003 to 10.6 % by weight of  $\beta$ -carotene,  
8                   2 to 7 % by weight of xylitol;  
9                   0.01 to 1 % of cetyl pyridinium chloride;  
10                  0.005 to 0.05 % by weight of disodium EDTA;  
11                  0.2 to 1.5 % by weight of flavoring agent, and  
12                  0.01 to 0.5 % by weight of sodium benzoate.

13                  **21.** A clear aqueous composition for topical application in the oral  
14 cavity of humans, the composition comprising:  
15 water;  
16 a water miscible pharmaceutically acceptable polyol;  
17 a pharmaceutically acceptable unsaturated fatty acid ester;  
18 a pharmaceutically acceptable surfactant, and  
19  $\beta$ -carotene, said  $\beta$ -carotene being in a micellized form within said  
20 composition.

1                   22. A composition in accordance with Claim 21 wherein the  
2 composition additionally comprises a pharmaceutically acceptable anti-  
3 oxidant.

4                   23. A composition in accordance with Claim 22 wherein the  
5 pharmaceutically acceptable anti-oxidant is d-alpha-tocopherol or a  
6 pharmaceutically acceptable derivative of d-alpha tocopherol having vitamin E  
7 activity.

8                   24. A composition in accordance with Claim 21 wherein the  
9 composition additionally comprises a compound having vitamin A activity.

10                  25. A composition in accordance with Claim 21 wherein the surfactant  
11 is polyethoxylated castor oil.

12                  26. A composition in accordance with Claim 21 wherein the polyol is  
13 glycerol.

14                  27. A composition in accordance with Claim 21 wherein the  
15 unsaturated fatty acid ester is ethyl linoleate.

16                  28. A composition in accordance with Claim 21 wherein the  
17 composition is a gel.

18                  29. A composition in accordance with Claim 21 wherein the  
19 composition comprises:

20                   10 to 50 % by weight water;

1                   5 to 40 % by weight of the water miscible pharmaceutically acceptable  
2 polyol;

3                   1 to 20 % by weight of the pharmaceutically acceptable unsaturated  
4 fatty acid ester;

5                   10 to 60 % by weight of the pharmaceutically acceptable surfactant,  
6 and

7                   0.03 to 9.0 % by weight of  $\beta$ -carotene.

8                   **30.** A composition in accordance with Claim 29 wherein the water  
9 miscible pharmaceutically acceptable polyol is glycerol;

10                   the pharmaceutically acceptable unsaturated fatty acid ester is ethyl  
11 linoleate, and

12                   the pharmaceutically acceptable surfactant is polyethoxylated castor oil.

13                   **31.** A composition in accordance with Claim 21 wherein the  
14 composition comprises:

15                   20 to 40 % by weight water;

16                   10 to 30 % by weight of the water miscible pharmaceutically  
17 acceptable polyol;

18                   1 to 15 % by weight of the pharmaceutically acceptable unsaturated  
19 fatty acid ester;

20                   20 to 40 % by weight of the pharmaceutically acceptable surfactant,  
21 and



0.3 to 3.0 % by weight of  $\beta$ -carotene.

**32.** A composition in accordance with Claim 31 wherein the water miscible pharmaceutically acceptable polyol is glycerol; the pharmaceutically acceptable unsaturated fatty acid ester is ethyl linoleate, and the pharmaceutically acceptable surfactant is polyethoxylated castor oil.

**33.** A composition in accordance with Claim 32 wherein the composition additionally comprises d-alpha-tocopherol and a compound having vitamin A activity.

**34.** A composition in accordance with Claim 33 wherein the composition is a gel.

**35.** A composition in accordance with Claim 21 wherein the composition comprises:

50 to 95 % by weight water;

1 to 10 % by weight of the water miscible pharmaceutically acceptable polyol;

0.01 to 2 % by weight of the pharmaceutically acceptable unsaturated fatty acid ester;

0.01 to 5 % by weight of the pharmaceutically acceptable surfactant, and

1 0.003 to 1.2 % by weight of  $\beta$ -carotene,  
2 1 to 10 % by weight of a pharmaceutically acceptable sweetener;  
3 0.01 to 2% of a pharmaceutically acceptable antibacterial agent;  
4 d -alpha tocopherol or a pharmaceutically acceptable derivative of d-  
5 alpha tocopherol having vitamin E activity;  
6 vitamin A palmitate or a pharmaceutically acceptable derivative of  
7 vitamin A palmitate having vitamin A activity;  
8 a pharmaceutically acceptable chelating agent;  
9 a pharmaceutically acceptable antifoaming agent;  
10 a flavoring agent, and  
11 a preservative.

12 36. A composition in accordance with Claim 35 wherein the water  
13 miscible pharmaceutically acceptable polyol is glycerol;

14 the pharmaceutically acceptable unsaturated fatty acid ester is ethyl  
15 linoleate;

16 the pharmaceutically acceptable surfactant is polyethoxylated castor  
17 oil;

18 the pharmaceutically acceptable sweetener is xylitol;

19 the pharmaceutically acceptable antibacterial agent is cetyl pyridinium  
20 chloride;

21 the pharmaceutically acceptable chelating agent is disodium EDTA,

1 and

2 the preservative is sodium benzoate.

3 37. A composition in accordance with Claim 36 wherein the  
4 composition is an oral rinse.

5 38. A composition in accordance with Claim 37 wherein the  
6 composition comprises:

7 75 to 95 % by weight water;

8 2 to 7 % by weight of glycerol;

9 0.01 to 0.5 % by weight ethyl linoleate;

10 0.01 to 1 % by weight polyethoxylated castor oil;

11 0.003 to 10.6 % by weight of  $\beta$ -carotene,

12 2 to 7 % by weight of xylitol;

13 0.01 to 1 % of cetyl pyridinium chloride;

14 0.005 to 0.05 % by weight of disodium EDTA;

15 0.2 to 1.5 % by weight of flavoring agent, and

16 0.01 to 0.5 % by weight of sodium benzoate.

17 39. A clear aqueous gel composition for topical application in the oral  
18 cavity of humans, the composition having been prepared by a process  
19 comprising the steps of:

20 admixing a suspension of  $\beta$ -carotene in edible oil with polyethoxylated

1 castor oil and heating said admixture to approximately 160 to 180 °C and  
2 agitating said admixture in said temperature range of 160 to 180 °C until a  
3 clear homogeneous solution is obtained;

4 thereafter cooling said admixture to approximately 130 to 135 °C and  
5 adding d-alpha-tocopherol, glycerol and ethyl linoleate to said admixture, the  
6 d-alpha-tocopherol, glycerol and ethyl linoleate being added to the admixture  
7 at such a rate of addition that the temperature of the resulting mixture is  
8 cooled to approximately 85 to 95 ° C;

9 maintaining the resulting mixture under agitation at 85 to 95° C until a  
10 clear homogeneous mixture is obtained;

11 thereafter adding under agitation water of approximately 55 to 60°C  
12 temperature and cooling the mixture under agitation until a clear homogenous  
13 product is obtained.

14 **40.** A clear aqueous gel composition in accordance with Claim 39  
15 comprising:

16 20 to 40 % by weight water;

17 10 to 30 % by weight of glycerol;

18 1 to 15 % by weight of ethyl linoleate;

19 20 to 40 % by weight of polyethoxylated castor oil;

20 0.3 to 3.0 % by weight of  $\beta$ -carotene.  
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